A neurodevelopmental approach to cognitive and behavioral assessment in epilepsy

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Epilepsy is a complex brain disorder that exerts distinct effects on neurodevelopment, behavior, and quality of life, depending on the timing of its onset across the life span. Seizures remain the defining feature of the clinical diagnosis of epilepsy. However, there has been a recent shift from classifying and understanding epilepsy based on seizure types to a more phenomenologic and syndromal approach, emphasizing a disruption of networks as a cause of seizures, in addition to well-known comorbidities in cognition and behavior.[1] While the development of functional neuroimaging has provided substantial insights into the composition and characteristics of neuroanatomical networks responsible for the development of seizures,[2] neuropsychological assessment, with the use of well-standardized neurocognitive and psychological tests, continues to provide the most validated and effective means of evaluating cognition and behavior in patients with epilepsy, in addition to other neurologic disorders.[3]

To date, the prevailing methods used in the neuropsychological assessment of patients with epilepsy were developed in a surgical context, where the profile of deficits in memory and executive functions is used to identify dysfunction in lateralized frontotemporal networks associated with the location of focal seizure onset.[3] While impairments in behavior and mood are frequently observed in patients with epilepsy, these impairments are often conceptualized as being in parallel to deficits in cognition, with little integration between the two. Similarly, while the age at seizure onset is a critical variable in the development of cognitive and behavioral comorbidities in epilepsy, there has been a lack of integration of neurodevelopmental factors into most models of neuropsychological disturbances in epilepsy.

In this issue of *Neurology*®, Rayner et al.[4] provide an important step toward developing a neurodevelopmental model of cognitive and behavioral impairment in epilepsy across the life span. Through their emphasis on the study of autobiographic memory, these authors identify distinct patterns of clinical variables, cognitive disturbance, and mood symptoms in adult patients with childhood-onset vs adult-onset epilepsy. The major implication from this study is that an integration of developmental, cognitive, and mood-related factors has the potential to help us identify more relevant phenotypes for classifying and treating behavioral disturbances in patients with epilepsy than what has been achieved over the years using a model limited to classification based on seizure types.

A unique feature of this study is the authors' focus on assessment of autobiographic memory over more standard neuropsychological testing approaches that focus on recall of word lists, stories, or figural designs. The primary findings are that patients with an early onset of epilepsy demonstrate impairments in autobiographic memory associated with other markers of chronic disease, including seizure frequency. In contrast, those patients with adult-onset epilepsy exhibit relationships among autobiographic memory, depression, and the presence of an MRI-identified lesion. Another implication, then, is that timing of disease onset determines the factors that are likely to influence memory impairment in a neurodevelopmentally appropriate manner. Early-onset epilepsy has the potential of altering neurodevelopmental networks responsible for normal memory function, while late-onset epilepsy produces memory dysfunction secondary to a psychiatric condition and lesional disruption of a fully developed neurocognitive network.

Results from a recent survey indicate that only 4% of neuropsychologists practicing in epilepsy specialty centers include an assessment of autobiographic memory as a standard component of the battery used for assessment of patients with epilepsy.[5] There are certainly a number of inherent challenges to assessing this type of memory in valid manner, with a common need to verify patient reporting of autobiographic information through contact with a collateral source. However, there also are a number of advantages to shifting focus to autobiographic memory, which utilizes a network of brain regions that can be altered by multiple factors, including psychological responses and neurodevelopmental disruptions.

Another important feature of this study lies in its emphasis on the delineation of cognitive phenotypes

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with the potential of enhancing approaches to classification and treatment of behavioral disorders in epilepsy. The identification of cognitive phenotypes in epilepsy is not new, as other investigators have identified cognitive phenotypes relevant to neuroanatomical findings from structural MRI.[6] Results from the current study diverge from previous research in the integration of mood and behavior in their phenotypic model. The implications for treatment are that educational and remedial interventions focused on modifying alterations in network development might be more appropriate for patients with early-onset epilepsy, whereas cognitive-behavioral approaches and pharmacologic interventions for depression may provide a more appropriate form of treatment for late-onset epilepsy, focusing on preventing a psychological maladjustment to seizures developing in adulthood.

As the authors note, the remarkable finding of this study is that the timing of disease onset alters the factors that are implicated in autobiographic memory impairments in epilepsy. If the field continues to develop an understanding of the neurologic, cognitive, and neuropsychiatric phenotypes of epilepsy, we may be able to identify the neural substrates that are involved and provide a better understanding of how epilepsy affects function across the life span.

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